OBJECTIVES: Anabolic-Androgenic Steroids (AAS) have been used for muscle mass development for over fifty years. The health outcomes of supraphysiologic doses of AAS have been debated, but most existing information pertains to men. This purpose of the study is to use the National Longitudinal Study of Adolescent Health (AddHealth) to elucidate health outcomes of AAS usage in women. **METHODS:** A cohort study of female AAS users were assessed in two time periods six years apart. Baseline descriptive statistics were used to describe age, income, race, drug use, education, and work performed for the sample. Follow up health outcomes include diabetes, heart disease, hyperlipidemia, anger, physician visit, use of medical care in the last year, Body Mass Index (BMI), blood pressure (BP), C-reactive protein, and HbA1C. Each dependent variable was tested in independent logistic regressions and in sensitivity tests using a MANOVA. **RESULTS:** The sample included 49 female respondents. Education was associated with a two-fold greater odds of AAS use comparing those who attended vocational school to those who attended college (OR=2.22, p=.03). Anger was associated with 88% greater risk of AAS use (OR=1.88, p=.04). HbA1c in the pre-diabetic range, while not statistically significant may be associated with AAS use (OR=1.85, p=.05). No other health outcomes were identified. **CONCLUSIONS:** This study contributes to the literature of female AAS use showing little in health care usage and long term health consequences. Anger is associated with male users but little research exists pertaining to this phenomenon in women. Elevated HbA1c is not commonly associated with AAS use, but due to the small sample size more research should assess AAS use among females.

PIH58

USER AND TREATMENT CHARACTERISTICS OF ORAL CONTRACEPTIVES IN THE EUROPEAN UNION

Bezemer ID[1], Verhamme KM[2], Gini R[3], Mosseveld M[2], Rijnbeek PR[2], Sturkenboom MC[2], Penning-van Beest FJA[1], Herings RMC[1]

[1]*PHARMO Institute for Drug Outcomes Research, Utrecht, The Netherlands,* [2]*EMC Rotterdam, Rotterdam, The Netherlands,* [3]*Agenzia regionale di sanità della Toscana, Firenze, Italy*

OBJECTIVES: As a basis for future safety evaluations of oral contraceptive (OC) use in Europe, current user and treatment characteristics were assessed in four European health care databases. **METHODS:** A descriptive retrospective database study was performed over 2009-2010 in GP databases from The Netherlands (IPCI), UK (THIN) and Italy (HSD) and linked pharmacy dispensing and hospital admission data from The Netherlands (PHARMO). Study follow-up started at the first OC prescription in 2009-2010 (users), one year after database entry or at Jan 1, 2009. Health indicators at start of follow-up included BMI and previous diagnosis of, or use of drugs for selected chronic conditions. Also, previous diagnoses of deep vein thrombosis, pulmonary embolism, cerebrovascular disease, myocardial infarction, breast cancer and cervical cancer were assessed. Treatment characteristics of OC included history of use, type of OC (chemical substance) used during 2009-2010 and switches or discontinuations. **RESULTS:** Among 4.9 million women, 14% had OC prescribed in 2009-2010. In The Netherlands and UK, 12-16% and in Italy 6% had a record of OC use. The prevalence of OC recorded prescription at January 1, 2010 was 81 per 1000 women of all ages and 271 per 1000 women aged 15-24, a much lower figure than what is recorded by surveys, probably due to switches between use and non-use and to reimbursement and/or prescription policies that reduce recording in GP databases. Among the non-users in 2009-2010, up to 22% had a history of OC recorded use. Little differences in health indicators were found between users and non-users in the databases where the information was available. **CONCLUSIONS:** Trends in health among European women in general also apply to OC users. However, OC use is not registered very well in health care databases which limits the possibilities of pharmacovigilance. Distribution channels and reimbursement policies vary, as well as recording in the databases.

PIH59

MEDICATION TREATMENT AND HEALTH CARE UTILIZATION FOR ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD) IN GERMANY

Schlander M[1], Banaschewski T[2], Trott GE[3], Schwarz O[4]

[1]*University of Heidelberg, Wiesbaden, Germany,* [2]*University of Heidelberg, Mannheim, Germany,* [3]*University of Wuerzburg, Aschaffenburg, Germany,* [4]*Institute for Innovation & Valuation in Health Care, Wiesbaden, Germany*

OBJECTIVES: To explore health care utilization and treatment patterns for attention-deficit/hyperactivity disorder (ADHD) in Germany, with particular emphasis on psychostimulant prescriptions. **METHODS:** The complete claims database of the organization of physicians registered with statutory health insurance (SHI) in Nordbaden/Germany was available for analysis, covering the total regional population enrolled in SHI (2.24 million lives). The dataset for years 2003 to 2009 was reorganized as to allow patient-centered evaluation. For calendar year 2009, 21,287 patients with ADHD (male, 15,108; female, 6,179; including 5,931 patients or 27.9% [male, 4,582; female, 1,349] with coexisting conduct disorder [F90.1 or a combination of F90 and F91 codes according to ICD-10]) were available for analysis. **RESULTS:** Preschool children (age 0-5 years) with ADHD were prescribed medication in very rare cases (1.6% in 2009) and after an average lead time of more than one year only. Most received some form of nonpharmacological therapy or were left untreated (42%). In contrast, 41% of children (age group 6-12 years, since 2003, continuously increasing from 32%) and 54% of adolescents (age group 13-17 years, rate remaining stable since 2006) were prescribed either stimulant (methylphenidate, MPH, or amphetamine) or nonstimulant (atomoxetine) drugs. Males and patients with concomitant conduct disorder were more likely to receive medication treatment. Modified-release MPH formulations were more widely used than immediate-release MPH. Overall use of medication increased steadily, from 32.2% of ADHD patients in 2003 to 39.9% in 2009, whereas its rate decreased over time in adult patients (declining from 38% in 2003 to 26% in 2009). – Upon individual review of all prescriptions of ADHD medication for members of the control group, no evidence was found supporting potentially inappropriate use of stimulant medication. **CONCLUSIONS:** Treatment patterns were highly age and gender specific. Except for preschoolers, therapeutic management of patients with ADHD relied heavily on drug treatment.

PIH60

TRENDS IN HOSPITAL ADMISSIONS AMONG MEN AND WOMEN ABOVE THE AGE OF 60 LIVING IN STOCKHOLM AND UPPSALA COUNTIES IN SWEDEN

Karampampa K[1], Andersson T[1], Drefahl S[2], Ahlbom A[1], Modig K[1]

[1]*Karolinska Institutet, Stockholm, Sweden,* [2]*Stockholm University, Stockholm, Sweden*

OBJECTIVES: To measure the change in the risk of first, second, and third hospitalization and the change in the proportion of hospitalization-free men and women above the age of 60 living in Stockholm and Uppsala counties in Sweden between 1972 and 2010. **METHODS:** Individuals were followed in national registers for hospitalizations and deaths from all causes between 1972 and 2010. Censoring occured at whichever of the following events appeared first; hospitalization (first, second, thrid), death, or December 31, 2010. Survival analysis was used to determine the proportion of hospitalization-free individuals. Discrete time logistic regression was used to obtain the the relative risk (RR) of first, second and third hospitalization. **RESULTS:** An increase in the proportion of hospitalization-free individuals over time was observed for both men and women; for example 87% more 82 year-old men, born in 1928, were free of hospitalizations since the age of 60 compared to those born in 1912. Between the years 1972 and 2010, the average annual decrease in the risk of first hospitalization after the age of 60 was 1% for both men (RR: 0.991, 95%CI: 0.991-0.992) and women. The average annual risk for hospitalization decreased for the second and thrid event as well; however the reduction was not significant. **CONCLUSIONS:** With the increase in the proportion of elderly in the population, the number of individuals with chronic diseases may increase, leading to higher demand for medical and social care. We have observed downward trends of the risk of first, second, and third hospitalization after the age of 60, which could be explained by a postponement of severe morbidity to higher ages. Focus on primary care and changes in inpatient care in Sweden may also partly exaplain the annual reduction in the risk of hospitalization.

PIH62

DO EMA AND FDA HAVE DIFFERENT OPINIONS/REQUIREMENTS IN TERMS OF PEDIATRIC STUDIES FOR SITAGLIPTIN (ALONE OR IN COMBINATION)?

Caron M[1], Emery MP[1], Maier W[2]

[1]*Mapi Research Trust, Lyon, France,* [2]*Mapi, London, UK*

OBJECTIVES: Since the implementation of Pediatric Regulations/Legislations in the USA (Pediatric Research Equity Act - PREA) and in Europe (Pediatric Investigation Plans - PIPs), product development programs should include pediatric studies. The objective of this study is to review opinions (EMA) and requirements (FDA) given by both agencies in the case of sitagliptin (alone and combined) for the treatment of diabetes mellitus in children. **METHODS:** The EMA and FDA websites were explored to: 1) Identify the products marketed under the INN of sitagliptin (alone or in combination), and 2) Identify the associated PIPs or PREA requirements. The search was performed on January 18, 2013. **RESULTS:** Eight products were marketed in Europe [i.e., sitagliptin (Januvia, Ristaben, Tesavel, Xelvia) and sitagliptin + metformin (Janumet, Efficib, Ristfor, Velmetia)]. Four products were authorized in the USA [i.e., sitagliptin (Januvia); sitagliptin + metformin (Janumet, Janumet XR); sitagliptin + simvastatin (Juvisync)]. The FDA and the EMA provided the same opinion for sitagliptin alone, i.e., deferred pediatric study for patients aged 11 to 16. The FDA and the EMA disagreed on sitagliptin + metformin. The EMA granted a waiver for all subsets of the pediatric population on the grounds that the specific medicinal product does not represent a significant therapeutic benefit over existing treatments, while the FDA required a pediatric study under PREA for the treatment of type 2 diabetes in pediatric patients aged 11 to 16. As for sitagliptin + simvastatin, the FDA grants a waiver on the grounds that the product does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients. **CONCLUSIONS:** The FDA and the EMA have similar opinions except for the combination sitagliptin + metformin. One reason could be the higher prevalence of type 2 diabetes mellitus in children in the USA as compared to Europe.

INFECTION – Clinical Outcomes Studies

PIN1

THE GEOGRAPHIC CORRELATION BETWEEN LYME DISEASE INCIDENCE AND DEGENERATIVE NEUROLOGICAL DISEASE MORTALITY: AN ECOLOGICAL STUDY

Veley KM, Malka ES

PPD, Morrisville, NC, USA

OBJECTIVES: The objective of the present study was to assess the geographic correlation between the incidence of Lyme disease (LD) and mortality due to certain degenerative neurologic diseases (DND) in the US. **METHODS:** For this ecological study, public data sources at the CDC were queried to quantify LD cases and DND deaths for the 5-year period 2002-2006. Alzheimer's disease, Parkinson's disease, and motor neuron disease were preselected as DND of interest. The separate datasets, for LD and DND, were combined by matching county and state names. Counties with at least 1 case of LD and at least 10 deaths due to DND were included in analyses. All analyses were performed in SAS. **RESULTS:** Of the 3141 counties of the US, 1372 reported at least 1 case of LD, 2742 reported at least 10 deaths due to DND, and 1339 met both conditions and were therefore included in analyses. The observed number of LD cases and DND deaths for a single county ranged from 1-6407 (mean: 78; median: 3) and 10-9207 (mean: 165; median: 55), respectively. The Spearman rank test indicated that there is a fair degree of correlation between LD incidence and DND mortality ($r=0.44$, $p<0.0001$). In sensitivity analyses, (1) excluding outliers, defined as observations $\geq 99^{th}$ percentile (LD>53; DND>1255), and (2) evaluating each disease separately, the correlation remained similar in magnitude and statistically significant (coefficient: 0.32-0.41; $p<0.0001$). **CONCLUSIONS:** There is a fair degree of correlation between LD incidence and DND mortality: US counties with a higher number of LD cases tend to have a higher number of

deaths due to DND. This study is limited by its ecological nature and more rigorous epidemiologic research is needed to elucidate the association between LD and DND.

PIN2

IMPACT OF HIGHLY ACTIVE ANTIRETROVIRAL THERAPY (HAART) REGIMEN ON ADHERENCE AND RISK OF HOSPITALIZATION IN VETERANS WITH HIV/AIDS

Rao GA[1], Sutton SS[1], Hardin J[2], Bennett C[2], Bramley T[3], D'Souza AO[3]
[1]*WJB Dorn VA Medical Center, Columbia, SC, USA,* [2]*University of South Carolina, Columbia, SC, USA,* [3]*Xcenda, Palm Harbor, FL, USA*

OBJECTIVES: High pill burden has been associated with poor adherence to HAART and adverse clinical outcomes. This study evaluated the impact of HAART as a single-tablet regimen (STR) and multiple-tablet regimen (MTR) on outcomes in HIV patients within the Veteran's Affairs (VA) system. **METHODS:** A retrospective, cohort study assessed patient VA dispensation data for HIV medications during the study enrollment period (7/1/2006 to 9/30/2011). Patients were assigned to the following cohorts: STR if they received a HAART regimen of a single tablet/day or MTR if they received a regimen of ≥2 tablets/day and no single tablet/day regimen during the enrollment period. Patients were followed from the index date (start of HAART regimen) until the earliest of treatment discontinuation, end of study period, or last date of health care-related activity (eg, VA benefits file or death). Hospitalization and adherence (medication possession ratio [MPR] ≥95%) were evaluated. Multivariate cohort differences in outcomes were controlled for using Cox-proportional hazard and logistic models; covariates were measured during a 6-month baseline period. **RESULTS:** In all, 15,602 patients (STR, n=6,191; MTR, n=9,411) met study criteria; average age of the study sample was 52 years. Both cohorts had similar CD4 counts (mean [SD]: 432.2 [282.8] vs 419.3 [280.9]; P=0.287) but significantly fewer patients receiving STR vs MTR had an undetectable viral load at baseline (42% vs 46%, P<0.001). During follow-up, significantly more STR patients were adherent compared to MTR patients (75% vs 55.7%, P<0.001). STR patients were also significantly less likely to experience hospitalization compared to MTR patients (26.8% vs 31.3%, P<0.001). After controlling for baseline covariates, STR patients had twice the odds of being adherent (OR: 1.98, P<0.001) and 31% lower hazard of experiencing hospitalization during follow-up (HR: 0.69, P<0.001). **CONCLUSIONS:** Treatment with STR compared to MTR improves adherence rates and decreases hospitalizations in patients with HIV/AIDS.

PIN3

A DECISION ANALYTIC MARKOV MODEL TO EVALUATE THE HEALTH OUTCOMES OF SOFOSBUVIR FOR PREVIOUSLY UNTREATED PATIENTS AND THOSE WITHOUT TREATMENT OPTIONS WITH CHRONIC HEPATITIS C VIRUS GENOTYPE 2 INFECTION

Younossi ZM[1], Gordon S[2], Saab S[3], Ahmed A[4], Cure S[5], Guerra I[5]
[1]*Inova Fairfax Hospital, Falls Church, VA, USA,* [2]*Henry Ford Hospital, Detroit, MI, USA,* [3]*David Geffen School of Medicine at UCLA, Los Angeles, CA, USA,* [4]*Stanford University, Stanford, CA, USA,* [5]*OptumInsight, Uxbridge, UK*

OBJECTIVES: Sofosbuvir (SOF) is a nucleotide polymerase inhibitor with excellent clinical efficacy in combination with ribavirin (RBV) for 12 weeks for patients who are chronically infected with hepatitis C virus (HCV) genotype 2. A decision-analytic Markov model evaluated the health outcomes of SOF+RBV compared with current treatment options for patients who are previously untreated, had no response to prior interferon treatment, or are unable to take interferon. **METHODS:** The analysis modeled 3 cohorts of chronic HCV genotype 2 patients with an average age of 50 and 25% with cirrhosis at the start of treatment followed-up to 100 years of age from a US third-party payer perspective. SOF+RBV for 12 weeks was compared with 1) pegylated interferon (PegIFN)+RBV for 24 weeks in the treatment-naïve patients; 2) PegIFN+RBV for 48 weeks in the treatment-experienced; and 3) no treatment in those unable to take interferon. Sustained virologic response (SVR) and adverse event rates were based on phase III clinical trials. Transition probability, utility, and cost estimates (in 2013 US dollars) were based on a literature review, public sources, and consensus by a panel of 4 hepatologists. **RESULTS:** In the treatment-naïve cohort, the SOF+RBV regimen resulted in an 83% decrease in the cases of liver disease complications including hepatocellular carcinoma, decompensated cirrhosis, liver transplant, and HCV-related death compared with PegIFN+RBV. The reduction of the listed liver disease sequelae was 59% in the treatment-experienced vs. PegIFN+RBV and 93% in the interferon-unable cohort vs. no treatment. The number needed to treat (NNT) with SOF+RBV rather than PegIFN+RBV to achieve one additional SVR was 6 in the treatment-naïve and 4 in the treatment-experienced cohorts. **CONCLUSIONS:** SOF+RBV was projected to yield better health outcomes in genotype 2 patients compared to PegIFN+RBV, largely driven by superior efficacy, and the potential to cure those who are unable to take interferon-based therapies.

PIN4

THE RELATIVE EFFICACY AND SAFETY OF SIMEPREVIR AND TELAPREVIR IN TREATMENT-NAÏVE HEPATITIS C INFECTED PATIENTS IN A JAPANESE POPULATION – A BAYESIAN NETWORK META-ANALYSIS

Bryden PA[1], Quigley J[1], Scott DA[1], Kuwabara H[2], Cerri K[3]
[1]*Oxford Outcomes Ltd., Oxford, UK,* [2]*Janssen Pharmaceutical KK, Tokyo, Japan,* [3]*Janssen Pharmaceutical NV, Beerse, Belgium*

OBJECTIVES: Simeprevir (SMV) is an oral, once-daily potent protease inhibitor for the treatment of chronic Hepatitis C genotype-1 infection (cHCV). In phase IIb/III RCTs conducted in Japan, SMV, in combination with peginterferon-α and ribavirin (PegIFN/RBV), demonstrated potent efficacy in cHCV genotype 1-infected patients relative to PegIFN/RBV and was generally safe and well-tolerated. Telaprevir (TVR) in combination with PegIFN/RBV is licensed for the treatment of cHCV in Japan. In the absence of head-to-head comparisons of TVR and SMV, we undertook a network meta-analysis (NMA) to examine the relative efficacy and safety of SMV and TVR in combination with PegIFN/RBV in a Japanese population. **METHODS:** A systematic review identified RCTs in Japanese treatment-naive patients with the above treatments and with the following endpoints: Sustained Virological Response (SVR), discontinuation of all medications (overall/due to Adverse Events (AE)), and incidence of anemia, rash (all grades) and pruritus-common adverse events of cHCV treatment. A Bayesian NMA was performed for all endpoints, assuming fixed study effects. Unpublished SMV studies meeting the inclusion criteria were obtained. **RESULTS:** Three studies met the inclusion criteria: 2 phase III RCTs (SMV n=183; TVR n=189), and 1 SMV phase IIb RCT (n=92). Baseline characteristics were generally comparable for all studies. SMV shows a higher odds ratio (OR) of achieving SVR versus TVR (OR 1.68 (0.66-4.26)). SMV shows a lower OR of discontinuation: overall 0.35 (0.12-1.00) and due to AEs 0.87 (0.23-3.34) versus TVR. SMV shows a lower OR of experiencing anemia 0.20 (0.07-0.56) and rash 0.42 (0.17-0.99) but a higher OR of experiencing pruritus 1.26 (0.46-3.47) versus TVR. The main limitation of this study is the small number of trials included in the analysis. **CONCLUSIONS:** In this indirect comparison, SMV, in combination with PegIFN/RBV, showed a favourable risk-benefit profile compared to TVR with PegIFN/RBV in Japanese treatment-naïve Hepatitis C infected patients.

PIN5

PUBLIC HEALTH IMPACTS OF PROBIOTICS IN CONTROLLING UPPER RESPIRATORY TRACT INFECTIONS IN FRANCE

Gerlier L[1], Lenoir-Wijnkoop I[2], Berdeaux G[1]
[1]*IMS Health HEOR, Vilvoorde, Belgium,* [2]*Utrecht University, Utrecht, The Netherlands*

OBJECTIVES: Two meta-analyses (York Health Economics Consortium [YHEC]; Cochrane) reported the beneficial effects of probiotics (live microorganisms which when administered in adequate amount confer a health benefit on the host). They demonstrated efficacy at reducing the duration and number of upper respiratory tract infections (URTI) and antibiotics use. The purchase of probiotics by consumers is likely to have positive externalities to the national health system and society. The aim of this analysis was to estimate the public health consequences of probiotics consumption, in France. **METHODS:** A 1/1,000 virtual age and gender standardized population was generated using a Markov model (TreeAge 2009). URTI risk factors were age, active/passive smoking, living in the community. Influenza like illness (ILI) and flu daily incidence rates came from Sentinelles, a practitioner network aimed at identifying flu outbreak. Epidemiologic data were used to differentiate cold, ILI and flu. One-day cycles were used over the 2011-2012 flu season. Probiotics effects came from two meta-analyses. Outcomes included numbers of URTIs days and episodes, antibiotics courses and sick leave days avoided with probiotics. **RESULTS:** According to YHEC data, probiotics reduced URTI episodes (average 7 days) by -0.77 days [-1.5;-0.04]. Extrapolating these results to the French population, probiotics would save 2.85 million URTI-days, the number of antibiotic courses would drop from 1,004,000 to 674,000 (difference about -330,000) and the number of sick leave days avoided in adults would be 653,000. According to Cochrane data, probiotics would reduce the probability to have an URTI episode by 0.58 [0.36;0.92] and antibiotic prescription by 0.67 [0.45;0.98]. The probiotic impact would become larger in terms of URTI-days avoided (-7.1 million), antibiotic courses (-509,000) and workdays lost (-1.2 million). **CONCLUSIONS:** The probiotics public health impact on URTI is significant at a national level even though this analysis was restricted to the 1% of patients visiting a practitioner.

PIN6

LONG-TERM OUTCOMES OF CHRONIC HEPATITIS C IN THE POPULATION OF NEWLY DIAGNOSED RUSSIAN PATIENTS

Ryazhenov VV, Sboyeva SG, Emchenko IV
I.M. Sechenov First Moscow State Medical University, Moscow, Russia

OBJECTIVES: To predict the future incidence of chronic hepatitis C in Russia and assess potential impact of the available antiviral therapies (pegylated interferon a-2a/a-2b or standard interferon a-2b combined with ribavirin) on long-term morbidity and mortality rates in the population of newly diagnosed Russian patients with chronic hepatitis C. **METHODS:** Based on the national epidemiologic data and published natural history studies, the prognostic Markov model was developed. Depending on the results of antiviral therapy, patients' flows over 25-year time frame were simulated. End points of interests included: the incidence of compensated and decompensated cirrhosis, hepatocellular carcinoma and cumulative time that patients will spend in each state, the number of patients, who will require liver transplantation, and HCV-related mortality rates. **RESULTS:** During years 2013-2017 about 276,000 new cases of chronic hepatitis C will be diagnosed in Russia. After 25 years since being diagnosed 130, 189 and 227 of 1,000 patients received pegylated interferon a-2a, pegylated interferon a-2b and standard interferon a-2b, respectively, will develop compensated cirrhosis. The cumulative time that patients will spend in compensated cirrhosis state will be 848, 1,218 and 1,482 patient-years, respectively. During the established time frame, there will be expected 25, 36 and 43 cases of hepatocellular carcinoma and 35, 51 and 62 HCV-related deaths. 28, 40 and 49 patients, respectively, will require liver transplantation. **CONCLUSIONS:** The findings from the present study provide the opportunity to plan volumes of medical care that will be required to Russian patients with chronic hepatitis C during 25 years since disease was first diagnosed. The treatment with pegylated interferon alfa-2a is considered the most preferable strategy due to considerably lower long-term morbidity and mortality rates as compared to pegylated interferon a-2b and standard interferon a-2b treatment.

PIN7

EPIDEMIOLOGY, TREATMENT OUTCOMES AND COSTS OF TREATING HEPATITIS C IN ROUTINE CARE – RESULTS FROM A LARGE MULTICENTER TRIAL

Stahmeyer JT[1], Rossol S[2], Bert F[2], Abdelfattah AM[2], Mauss S[3], Heyne R[4], John C[5], Pape S[6], Schober A[7], Teuber G[8], Bruch HR[9], Zehnter E[10], Hueppe D[11], Pfeiffer-Vornkahl H[12], Alshuth U[13], Krauth C[1]
[1]*Hannover Medical School, Hannover, Germany,* [2]*Krankenhaus Nordwest, Frankfurt a.M., Germany,* [3]*Center for HIV and Hepatogastroenterology, Duesseldorf, Germany,* [4]*Liver and study center Checkpoint, Berlin, Germany,* [5]*Center of Gastroenterology, Berlin, Germany,* [6]*Center of Gastroenterology, Paderborn, Germany,* [7]*Center of Gastroenterology, Goettingen, Germany,*